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# Refobacin Concentration in Blood Serum, Urine and Wound Secretion: A Comparative Study of Refobacin-Palacos and Implast- Gentamicin in Total Hip Replacement

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## Introduction

In the field of orthopaedic surgery the possibility of treatment for severe dysfunction of the joint can no longer be conceived without the innovation of alloarthroplasty. The value of an operation method is ultimately determined by the late results and specific possibilities of complication. A critical complication in the case of total endoprosthesis is the eventuality of loosening.

With this in mind we carried out tests within a small area of the research on bone cement.

## Materials and Methods

The Gentamicin concentrations in serum, urine and wound secretions of 9 patients whose endoprostheses were implanted with Refobacin-Palacos were examined. These values were compared with the analyses of 8 patients whose endoprostheses were implanted with Implast-Gentamicin.

The analysis of serum and urine tests was carried out by means of fluorescence-polarization with the TDX machine of the Abbott Company. The statistical indication limit was specified by the maker as 0.16  $\mu\text{g/ml}$  which was corroborated in our testing. At the beginning of the testing we recalibrated the machine.

Specifically for the urine tests, several analyses were necessary to reach the measuring range of the machine by adequate dilutions. All the results are mean values of double analysis.

The wound secretion tests were checked microbiologically on Gentamicin activity by means of agar diffusion. The indication limit was 0.1  $\mu\text{g/ml}$ .

## Results

Figure 1 shows the mean values of Gentamicin concentration in the wound secretions.

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Key words: Total hip replacemant, Antibiotics concentration and excretion.

索引語: 股関節全置換術, 抗生物質生体内濃度.

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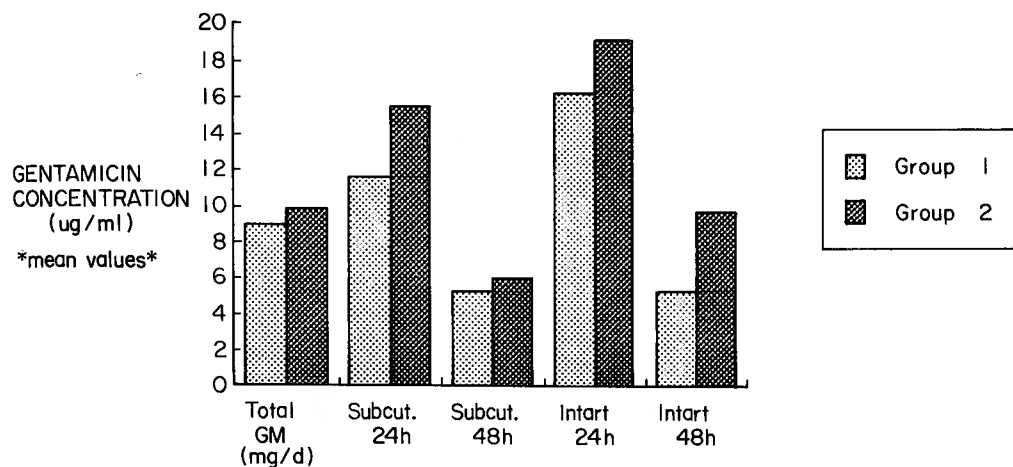


Fig. 1. Wound secretion

Group 1 is the Refobacin-Palacos group, and Group 2 shows those with Implast-Gentamicin.

In Figure 2 the mean values of the total precipitation in the urine on each postoperative day are shown.

Especially interesting were the mean values of the blood serum tests as they are shown in Figure 3. At all times the blood serum tests of the Implast-Gentamicin group were higher than those of the comparison group.

In Figure 4 the blood serum tests are shown graphically in the median for both groups. Group 2 shows clearly higher values. In Group 1 the Gentamicin precipitation in the urine is, at all measured times, higher and reaches, on the first postoperative day, values nearly double those of Group 2 (Fig. 5).

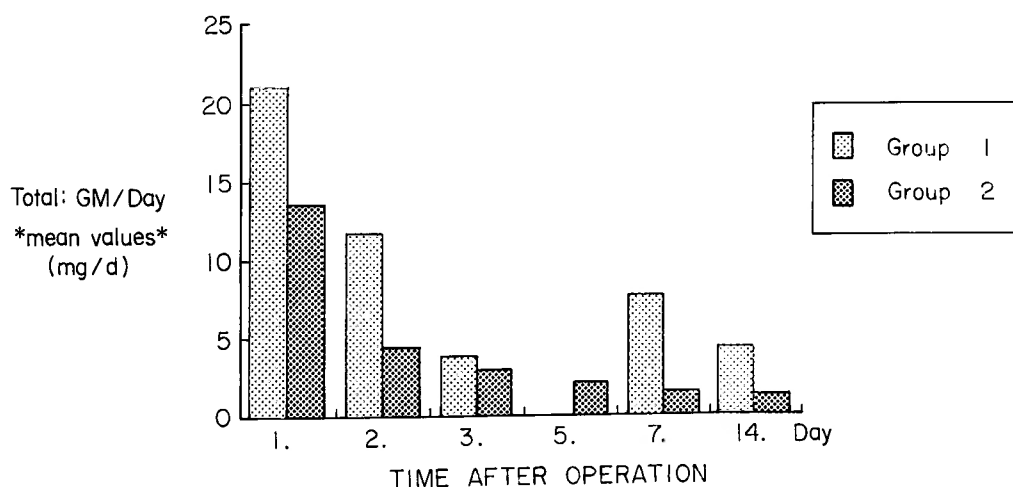


Fig. 2. Total precipitation per day

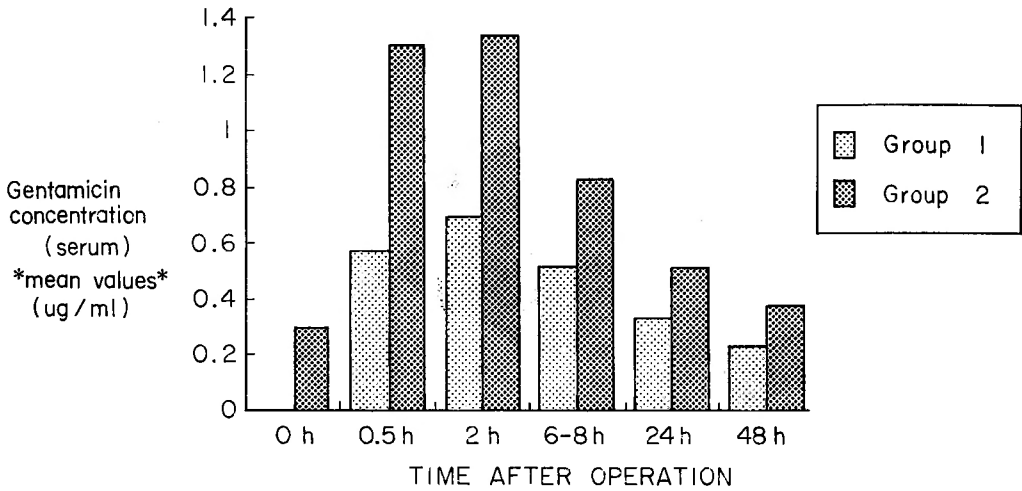


Fig. 3. Blood serum test

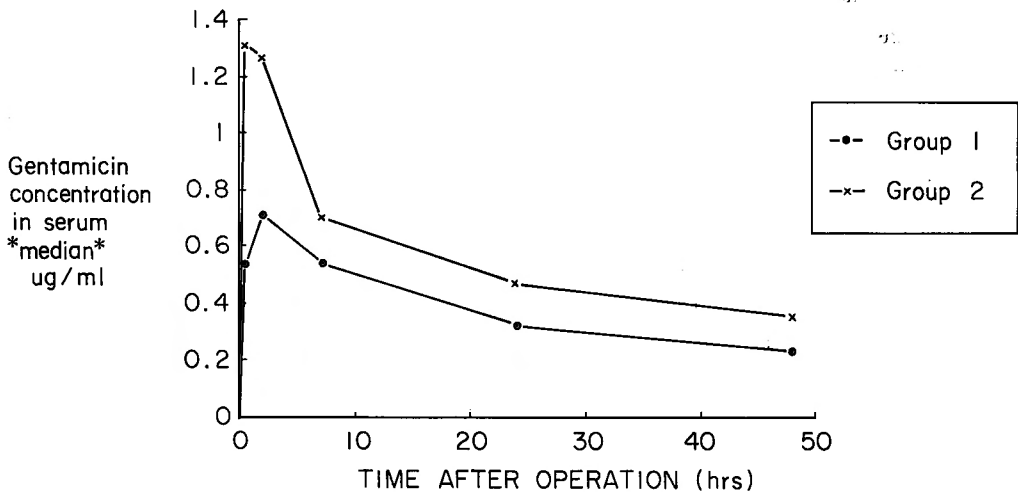
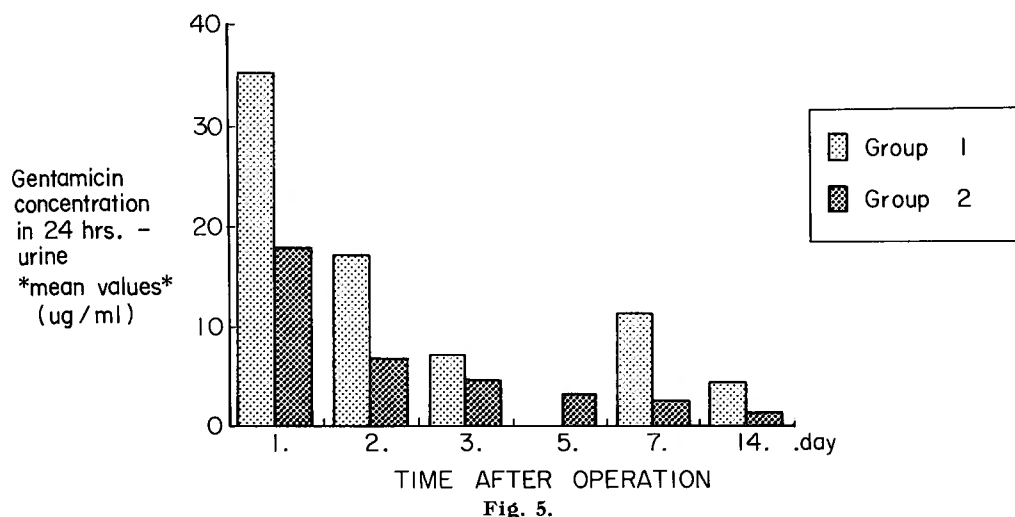


Fig. 4. Blood serum test, postoperative

### Discussion

In the König-Ludwig-Haus Orthopaedic University Hospital in Würzburg, a total of 1,729 hip prostheses were implanted in the period from October, 1968 to August, 1979. The types of prostheses used are shown in Table 1. In the same period of time, 110 prosthesis exchange operations on 105 patients (48 male and 57 female) were carried out successfully in our hospital. Of the 110 prosthesis exchange operations, 90 cases were due to aseptic and 20 due to septic loosening of the prosthetic device.

In 81 patients (45 male and 36 female), all 84 hip prostheses had to be removed without replacement in the period from October, 1968 to August, 1979 (total 1,729 hip prostheses). The results of the operations were Girdlestone hips.



Many different ways have been tried to control the problem of prosthesis loosening<sup>3,4</sup>. On one hand it is desirable to secure a stable anchorage without cement, and impaction of the bone and the implanted prosthesis by means of the best biomechanical design of the prosthesis. For this a biocompatible material for the prosthesis is also necessary. On the other hand, it should be attempted to advance closer to a solution of the problem by means of improvement in the operation technique as well as the improvement of the bone cement<sup>1,2,5</sup> (Table 2).

As in all other bone cements, the newly developed bone cement Implast-Gentamicin is a product made of polymethyl methacrylate. Because of the special composition of Implast, the quality was improved in some areas compared to conventional bone cements.

The maximum hardening temperature is lowered to 45°–50°C and the intrusion is increased to 5–9 mm, measured according to DIN-ISO 5833. The proportion of 23% monomeric methacrylic acid methyl-ester is about 10% lower than that of comparable bone cements. The concentration of residuum monomers is reduced about 90% as compared with conventional bone cements.

Table 1.

| <i>Type of Prosthesis</i>    |                    |       |
|------------------------------|--------------------|-------|
| Müller-Charnley              | (1969 until 1975)  | 894   |
| Weller-Aesculap              | (1975 until today) | 591   |
| McKee-Farrar                 | (1970 until 1973)  | 33    |
| Weber-Huggler                | (1971 until 1974)  | 49    |
| Ceramic Prosthesis—Lindenhof | (1976 until 1978)  | 44    |
| Shell Prosthesis (Wagner)    | (1976 until today) | 44    |
| Head Endoprosthesis (Moore)  | (1969 until today) | 71    |
| Others                       |                    | 13    |
| TOTAL                        |                    | 1,729 |

Table 2.

*Loosening of Prosthesis:*

|                   | Exchange Operation | Removal |
|-------------------|--------------------|---------|
| Total             | 110                | 84      |
| Septic Loosening  | 20                 | 59      |
| Aseptic Loosening | 90                 | 25      |

The results of the Implast-Gentamicin Group (Group 2) reflect, in comparison to Group 1, a positive bioequivalence with an overall high Gentamicin concentration in wound secretions and blood serum. In Group 2 the relative bioavailability of the Gentamicin consisting of bone cement, amounts in the blood serum to  $170.8\% \pm 46.54$  (median), respectively  $179.9\% \pm 31.71$  (mean values) in comparison to the reference preparation. On the first day the renal elimination in Group 1 was much more distinct than in Group 2. In Group 2 the relative total precipitation amounts to  $45.5\% \pm 11.52$  (median) and  $45.9\% \pm 23.89$  (mean values) in comparison to the reference group. These optimistic data must be qualified since they show only provisional results, gained with only a small number of patients. Furthermore, all values must be cleared according to the individual Creatinin-Clearance. However these provisional results allow a well-founded optimism for further testing.

### Conclusion

The value of the Gentamicin concentrations in serum, urine and wound secretions of 9 patients whose total prosthesis were implanted with Refobacin-Palacos was compared with the analysis of 8 patients whose endoprostheses were implanted with Implast-Gentamicin. The following results were obtained.

- 1) The Implast-Gentamicin group reflected a positive bioequivalence with an overall high Gentamicin concentration in wound secretions and blood serum with relative bioavailability of the Gentamicin.
- 2) The renal elimination in Refobacin-Palacos group was much more distinct than in Implast-Gentamicin group, especially on the first day.

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## 和文抄録

## 股関節全置換術における Refobacin 濃度に関する研究

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股関節全置換術における合併症の1つとして人工関節の loosening がある。この人工関節のゆるみの原因として感染あるいはメカニカルな因子があげられている。人工関節の固定材料としての骨セメント使用に関しても種々の議論がなされている。一方骨セメント剤も最近種々の改良が行われている。本論文ではその改良型である Implast-Gentamicin および Refobacin-Palacos を用いた全置換術について、血清・尿・創部における術後の Gentamicin 濃度に関して比較検討を

行った。対象患者は Refobacin-Palacos 使用例9例、Implast-Gentamicin 使用例8例である。それによると(1) Implast-Gentamicin 群においては創部浸出液および血清に比較的高濃度の Gentamicin を検出し、良好な生体内当量と利用率を認めた。(2) Refobacin-Palacos 群においては術後第1日目に腎よりの高濃度の排出を認めた。今後なお生体力学的な骨セメントの効果の研究に加えて、このような生化学的な性質の研究も進めていく必要がある。